In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-530V
Filed: September 3, 2020
PUBLISHED

SHAUNYIA BRUNSON, on behalf of T.A., deceased.,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Sudden Infant Death Syndrome (SIDS); Dismissal; Insufficient Proof

Mark Sadaka, Mark T. Sadaka, LLC, Englewood, NJ, for petitioner.
Heather Lynn Pearlman, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On April 14, 2017, petitioner, Shaunyia Brunson, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012)[2] on behalf of her minor child, T.A. Petitioner alleges that the rotavirus, DTaP, HIB, IPV, and pneumococcal 13 vaccinations, administered on May 28, 2015, caused or significantly contributed to T.A.'s death, categorized as a case of Sudden Infant Death Syndrome ("SIDS") on June 2, 2015. (ECF No. 1.) On February 14, 2020, petitioner filed a motion for a ruling on the written record. (ECF No. 46.) For the reasons set forth below I find that petitioner is not entitled to compensation.

[1] Because this decision contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec' of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program fact finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

In her petition, petitioner initially characterized T.A.'s alleged injury as a "sudden death" that was caused-in-fact or significantly aggravated by her May 28, 2015 vaccinations. (ECF No. 1, p. 1.) Petitioner's expert later more specifically termed T.A.'s death as a case of Sudden Infant Death Syndrome or "SIDS." (Ex. 7, p 5.) Since SIDS is not listed on the Vaccine Injury Table, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.[3]

[3] Although petitioner also incorporated a claim of significant aggravation in her petition, the analysis for a significant aggravation caused-in-fact by vaccination (the *Loving* test) incorporates and extends the *Althen* causation-in-fact analysis described above to include three additional factors. *Loving v. Sec'y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (Fed. Cl. 2009) (combining the first three *Whitecotton* factors for claims regarding aggravation of a Table injury with the three *Althen* factors for off table injury claims to create a six-part test for off-Table aggravation claims); *see also W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013)(applying the six-part *Loving* test.). The additional *Loving* factors require petitioner to demonstrate aggravation by showing: (1) the vaccinee's condition prior to the administration of the vaccine, (2) the vaccinee's current condition, and (3) whether the vaccinee's current condition constitutes a "significant aggravation" of the condition prior to the vaccination. *Id*. Here, T.A.'s pre- and post- vaccination conditions are essentially undisputed. There is little question that T.A. experienced a death deemed as SIDS five days after vaccination. Moreover, the pre-existing condition that would underlie petitioner's significant aggravation claim is a hippocampal abnormality the fact (but not significance) of which is also undisputed. This abnormality is discussed in section VI(b)(i) below, relative to *Althen* prong two because the presence of an underlying vulnerability is also a significant part of petitioner's expert presentation seeking to explain a logical sequence of cause and effect leading to T.A.'s death. For all the reasons discussed below, petitioner's inability to meet the *Althen* test is dispositive regardless of whether this claim is conceptualized as one of causation-in-fact or significant aggravation. In her motion for a ruling on the record, petitioner discussed this case in the context of an *Althen* analysis. (ECF No. 46.)

II. Prior SIDS Cases in This Program and Guidance from the Federal Circuit

SIDS is not an injury or disease in itself. (Ex. 7, p. 8.) Generally, all infant deaths that are sudden and unexpected are termed as such – "Sudden Unexplained Infant Death" or "SUID." The term SIDS is further applied to those SUID cases that remain unexplained following an autopsy, investigation, and clinical history review. (Hannah C. Kinney & Bradley T. Thach, *The Sudden Infant Death Syndrome*, 361 N. ENGLAND J. MED. 795, 797 (2009) (Ex. D, p. 2).) The first standard definitions of SIDS was advanced by the National Institute of Health in 1969. Under that definition SIDS represents the "sudden death of an infant or young child, which is unexpected by history, and in which a thorough post mortem examination fails to demonstrate an adequate cause of death." (Kinney & Thach, *supra*, at Ex. D, p. 1.) As of the mid-to-late 2000s, SIDS has an incidence rate in the United States of 0.57 out of 1,000. (*Id*.) About 80% of SUID cases are classified as SIDS. (*Id*. at 2.)

Research by Dr. Hannah Kinney revealed that the serotoninergic network in medulla oblongata of infants suffering SIDS is frequently defective. (Ex. 7, p. 8; *see also* Hannah C. Kinney et al., *The Brainstem and Serotonin in the Sudden Infant Death Syndrome*, 4 ANN. REV. PATHOLOGY 517 (2009) (Ex. 28).) Specifically, the serotoninergic network is a network by which arcuate nuclei use serotonin (5-hyrdoxytryptamine or "5-HT") as a neurotransmitter in the regulation of respiratory effort, including recovering from apnea and hypercarbia. (*Id*.) If the infant's serotoninergic network is underdeveloped or defective and the infant experiences a normal episode of apnea or an event which causes hypercarbia during sleep, the defective network cannot trigger the neurons which stimulate arousal and increased breathing effort for recovery from that apnea or hypercarbia, and the infant dies. (*Id*.) Severe deficits in the number of 5-HT receptors exist in 70-90% of SIDS cases. (*Id*. at 9.)

This discovery helped give rise to the "Triple Risk Theory" (also referred to herein as the "Triple Risk Model"). (Ex. 7, p. 9.) First proposed in 1994, the Triple Risk Model identifies three factors that combine to result in SIDS: (1) an underlying vulnerability; (2) a critical developmental period; and (3) an exogenous[4] stressor. (Kinney & Thach, *supra*, at Ex. D, p. 2; Kinney et al, at Ex. 28, pp. 3-4.) This theory hypothesizes that in an infant with a serotoninergic network vulnerability, in the appropriate critical developmental period, an acute "stressor" or combination of stressors can cause apnea or hypercarbia leading to death, because of the failure of the network to stimulate the normal arousal inducing response. (Ex. 7, p. 9.)

There have been a significant number of prior cases in this Program that have addressed allegations that one or more childhood vaccines caused or contributed to a SIDS-labeled death. Generally, such cases have been dismissed in the first instance by the presiding special masters for insufficient evidence that any vaccine played a causal role in the death. *See*, *e.g.*, *Olasvicky v. Sec'y of Health & Human Servs*., No. 17-

[4] "Exogenous" refers to something "developed or originating outside the organism." (*Dorland's Illustrated Medical Dictionary*, p. 652 (33rd ed., 2019).)

1806V, 2019 WL 2881009 (Fed. Cl. Spec. Mstr. June 4, 2019); *Nunez v. Sec'y of Health & Human Servs*., No. 14-863V, 2019 WL 2462667 (Fed. Cl. Spec. Mstr. Mar. 29, 2019), review denied 144 Fed. Cl. 540 (2019); *Frady v. Sec'y of Health & Human Servs*., No. 16-148V, 2017 WL 5379391 (Fed. Cl. Spec. Mstr. Sept. 20, 2017); *Pelton v. Sec'y of Health & Human Servs.*, No. 14-674V, 2017 WL 1101767 (Fed. Cl. Spec. Mstr. Feb. 27, 2017); *Jewell v. Sec'y of Health & Human Servs.*, No. 11-138V, 2016 WL 5404165 (Fed. Cl. Spec. Mstr. Aug. 29, 2016); *Copenhaver v. Sec'y of Health & Human Servs.*, No. 13-1002V, 2016 WL 3456436 (Fed. Cl. Spec. Mstr. May 31, 2016), review denied, 129 Fed. Cl. 176 (2016); *Lord v. Sec'y of Health & Human Servs.*, No. 12-255V, 2016 WL 806818 (Fed. Cl. Spec. Mstr. Feb. 9, 2016); *Cozart v. Sec'y of Health & Human Servs.*, No. 00-590V, 2015 WL 6746616 (Fed. Cl. Spec. Mstr. Oct. 15, 2015), review denied, 126 Fed. Cl. 488 (2016); *Waterman v. Sec'y of Health & Human Servs.*, No. 13-960V, 2015 WL 4481244 (Fed. Cl. Spec. Mstr. June 30, 2015), review denied 123 Fed. Cl. 564 (2015); *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-651V, 2013 WL 4476750 (Fed. Cl. Spec. Mstr. Jul. 26, 2013); *Bigbee v. Sec'y of Health & Human Servs.*, No. 06-663V, 2012 WL 1237759 (Fed. Cl. Spec. Mstr. Mar. 22, 2012); *Nordwall v. Sec'y of Health & Human Servs.*, No. 05-123V, 2008 WL 857661 (Fed. Cl. Spec. Mstr. Feb. 19, 2008); *Doe/11 v. Sec'y of Health & Human Servs.*, 2008 WL 649065 (Fed. Cl. Spec. Mstr. Jan. 31, 2008); *Heller v. Sec'y of Health & Human Servs*., No. 96-797V, 1998 WL 408612 (Fed. Cl. Spec. Mstr. June 22, 1998).

In some instances, the parties have litigated whether SIDS presents an alternative cause of what petitioners otherwise alleged to have been a vaccine-caused death. *See, e.g.*, *Doe/11 v. Sec'y of Health & Human Servs.*, 601 F.3d 1349, 1351 (Fed. Cir. 2010) (holding that "the special master did not commit legal error in considering evidence of SIDS, an allegedly alternative cause. Nothing in the Vaccine Act prohibits the government from presenting evidence that the petitioner's injury was due to "factors unrelated" to the vaccine (here, SIDS)."). Significant to this case, however, many of these prior cases have directly addressed at length allegations that one or more vaccines directly caused or contributed to a child's death within the framework of the Triple Risk Model of SIDS. In these prior decisions special masters found that attempts to establish vaccination as an exogenous stressor under the accepted Triple Risk Model of SIDS were unpersuasive. *See, e.g.*, *Jewell,* 2016 WL 5404165 at *13; *Copenhaver,* 2016 WL 3456436 at *12-13; *Lord,* 2016 WL 806818 at *14; *Cozart,* 2015 WL 6746616 at *13.

In *Boatmon v. Secretary of Health & Human Services*, however, the special master concluded that a child's sudden, unexplained death was consistent with SIDS and that his death was caused, in part, by his vaccinations. No. 13-611V, 2017 WL 3432329 (Fed. Cl. July 10, 2017*), review granted, decision rev'd*, 138 Fed. Cl. 566 (2018), *aff'd on other grounds*, 941 F.3d 1351 (Fed. Cir. 2019). The *Boatmon* petitioners presented a theory through their expert, Dr. Miller (who also opines in this case), that vaccines produce a cytokine response that can act as an exogenous stressor on the 5-HT network to cause SIDS within the Triple Risk Model. The special master explained:

> I have concluded that petitioners have presented sufficient evidence and testimony to entitle them to compensation in the Vaccine Program. I have not concluded that vaccines present a substantial risk of SIDS. In fact, the evidence is to the contrary. The vast majority of vaccine recipients do not succumb to SIDS. Under the multi-factorial analysis of the Triple Risk Model, it is theorized that the ultimate fatal event may occur when multiple factors converge during this vulnerable period to cause death when one stressor acting alone may not have.

Id. at *42. However, respondent successfully moved for review of the special master's decision in *Boatmon*. On July 3, 2018, the Court of Federal Claims reversed and vacated the special master's decision and dismissed the petition. *Boatmon v. Sec'y of Health & Human Servs.*, 138 Fed. Cl. 566 (2018).

Citing *Jewell*, *Copenhaver*, *Lord*, and *Cozart*, *supra*, the Court was critical of the special master for disregarding prior decisions by other special masters that uniformly found the same or similar theories unpersuasive. *Boatman*, 138 Fed. Cl. at 571. More significantly, however, the Court found that the special master had erred by impermissibly lowering petitioners' burden of proof. *Id*. at 571-72. Specifically, the Court explained:

> This departure from the conclusions of other Special Masters can only be explained by improper application of the standard of proof required in vaccine cases. While scientific certainty is not required to establish causation under the Vaccine Act, the theory must be supported by a "sound and reliable" medical or scientific explanation. *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). In *Moberly*, 592 F.3d at 1322, the Federal Circuit noted that a Petitioner must provide a "reputable medical or scientific explanation" for causation, and that this standard requires more than mere "plausibility," which is "not the statutory standard." In the case at bar, the theory embraced by the Special Master has not been accepted by any other experts in the field of SIDS research.

Id.

The *Boatmon* petitioners appealed to the U.S. Court of Appeals for the Federal Circuit. However, on November 7, 2019, the Federal Circuit affirmed the Court of Federal Claims. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351 (Fed. Cir. 2019). Although the Federal Circuit noted that special masters are not obligated to rely on a *Daubert* analysis and are not obligated to distinguish the decisions of other special masters, the Court agreed with the Court of Federal Claims that the special master had impermissibly lowered petitioners' burden of proof. *Id*. at 1358-59. Pertinent to this case, the Federal Circuit explained that, while petitioners are not required to demonstrate causation with scientific certainty, to satisfy *Althen* prong one, petitioners must present expert opinion that provides a scientific explanation that is "sound and reliable." *Id*. The Federal Circuit stressed that theories that are merely "plausible" do

not meet that standard. *Id.* at 1359. With regard to the Triple Risk Model of SIDS, the Federal Circuit held that petitioners' expert's theory that vaccination could act as the exogenous stressor pursuant to that theory was not sound and reliable. *Id*. at 1361.

First, the Federal Circuit explained that "outside of Vaccine Act litigation, vaccinations have not been identified as an exogenous stressor for SIDS." *Id*. The Federal Circuit noted that petitioners' "extension of the Triple Risk Model to include vaccination-induced cytokine activity in the list of exogenous stressors" was based on "nothing more than the assertion of [petitioners' expert] Dr. Miller." *Id*. at 1360-61. Accordingly, the Federal Circuit concluded that "[t]he Special Master erred in adopting an unsound and unreliable theory that constitutes a significant extension of the Triple Risk Model in the absence of any indicia of reliability." *Id*. at 1362.

Second, the Federal Circuit determined that petitioners had "failed to show by a preponderance of the evidence that vaccinations cause cytokines to provoke an abnormal brainstem serotonin response or otherwise cause or contribute to a SIDS death." *Id*. The Federal Circuit discussed three studies (Frøen, Stoltenberg, and Brambilla) presented by petitioners as supportive of Dr. Miller's theory; however, the Federal Circuit concluded that "these studies do not provide support for Dr. Miller's proposed theory because they do not show that that cytokine activity is capable of impacting the brain's 5–HT system in the manner Dr. Miller claims or that vaccinations are capable of producing such cytokine activity in the brain." *Id*. at 1360-62.

With regard to the remaining *Althen* prongs, the Federal Circuit's guidance in *Boatmon* is limited to a discussion, relative to *Althen* prong two, of a brain stem abnormality alleged in that case to constitute an underlying vulnerability consistent with the Triple Risk Model. 941 F.3d at 1362-63. In that case, there was no physical evidence establishing the presence of a brain stem abnormality and the conclusion that the *Boatmon* child was in a vulnerable state was based in large part on statistical evidence that such an abnormality is present in 50-70% of SIDS cases. *Id*. The Federal Circuit found that conclusion to be error. *Id*.

Special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Human Servs.,* 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the expertise and experience to know the type of information that is most probative of a claim"). Nonetheless, special masters are not bound by the prior decisions of other special masters. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). In contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). However, the Federal Circuit has also stressed that "[c]ausation in fact under the Vaccine Act is ... based on the circumstances of the particular case." *Boatmon*, 941 F.3d at 1358-59 (quoting *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cr. 1994). Accordingly, Federal Circuit precedents do not

automatically control the outcome of subsequent cases even when they involve the same injury. *See, e.g.*, *Sanchez v. Sec'y of Health & Human Servs.*, 809 Fed. Appx. 843, 851-52 (Fed. Cir. 2020) (citing back to a prior Federal Circuit holding in *Paluck v. Secretary of Health & Human Services* involving the same injury and noting that "while there are substantial parallels between this case and *Paluck*, the differences between the two cases are such that the outcome of this case is not dictated by *Paluck*.").

In *Downing-Powers v. Secretary of Health & Human Services*, I previously addressed the significance of the *Boatmon* decision in another SIDS case involving an expert opinion by Dr. Miller.[5] No. 15-1043V, 2020 WL 4197303 (Fed. Cl. Spec. Mstr. June 2, 2020). In that case I found, contrary to petitioners' contentions, that Dr. Miller's opinion in that case was still, as in *Boatmon*, based on his own *ipse dixit* extension of the Triple Risk Model to include vaccines as an exogenous stressor. *Id.* at *11. Moreover, I found that, despite the finding of certain animal model studies, Dr. Miller did not persuasively demonstrate that peripheral cytokine activity due to vaccination would have the type of effect *in vivo* on the serotoninergic network posited by the Triple Risk Model. *Id.* at *14.

In this case, as he did in *Downing-Powers*, respondent characterizes the Federal Circuit decision in *Boatmon* as having a "binding nature" and argues petitioner "has not successfully distinguished her causation theories from those that were rejected in *Boatmon*." (ECF No. 47, p. 1-2.) Respondent emphasizes that Dr. Miller's theory of vaccine causation has been discussed by the Federal Circuit and has been found to be unreliable and insufficient to form the basis of finding entitlement in the Vaccine Program. (*Id*. at 1.)

In making her motion for a ruling on the record, petitioner in this case indicated that she

> is a mother who is tired of reliving the pain of losing her infant and does not want to drag her family through something that will more likely than not result in a negative ruling considering *Boatmon*. This is an important distinction. She is not filing a motion for a ruling on the record because of the *Boatmon* decision. Mrs. Brunson is filing a motion for a ruling on the record because of the implications of that decision.

(ECF No. 48, p. 2.)

More recently, and subsequent to the parties' submission of their briefs in this case, the Federal Circuit issued an additional decision further addressing Dr. Miller's extension of the Triple Risk Model to encompass vaccinations. *Nunez v. Sec'y of Health & Human Servs.*, No. 2020-1021, 2020 WL 5087990 (Fed. Cir. Aug. 28, 2020). Unlike in *Boatmon*, the *Nunez* special master had rejected Dr. Miller's opinion. The Federal

[5] In that case, petitioners also presented an additional opinion by Dr. Lawrence Steinman. Dr. Steinman's opinion was considered both separately and as further support for Dr. Miller's opinion. *Downing-Powers v. Sec'y of Health and Human Servs.*, No. 15-1043v, 2020 WL 4197303 (Fed. Cl. Spec. Mstr. June 2, 2020).

Circuit indicated that "the record reflects no major advances in the state of medical knowledge concerning a relationship between vaccinations and SIDS in the short time that has passed since this court decided *Boatmon* less than a year ago. And we have no basis to conclude that studies from 2006 and 2014 are the type of new evidence that is so indicative of the reliability of Dr. Miller's theory that it makes the Special Master's factual findings arbitrary and capricious for having rejected it." *Id.* at *2.

III. Procedural History

Petitioner filed her petition on April 14, 2017. (ECF No. 1.) The case was initially assigned to Special Master Laura Millman, who has since retired. (ECF No. 4.) Subsequently, petitioner filed medical records and a Statement of Completion. (ECF Nos. 7, 10, 11.) After the initial status conference, petitioner intended to have a pathologist review paraffin tissue blocks and provide an expert report. (ECF No. 13.)

On July 13, 2018, petitioner filed an expert report from Dr. Douglas C. Miller. (ECF No. 24; Ex. 7.) Thereafter, respondent filed his Rule 4(c) report, arguing that the evidence presented did not meet petitioner's burden and recommending against compensation. (ECF No. 28.) Respondent then filed an expert report from Dr. Andrew MacGinnitie on December 21, 2018. (ECF No. 30; Ex. A.) Respondent intended to additionally file an expert report from Dr. Sanda Alexandrescu; however, petitioner filed a motion to suspend proceedings to await the outcome of *Boatmon* appeal at the Federal Circuit. (ECF No. 34.) Special Master Millman granted petitioner's motion and stayed proceedings for one month.

On May 3, 2019, petitioner filed a second motion to suspend proceedings, arguing that the outcome on the appeal in *Boatmon* will influence the direction that petitioner takes on her case. (ECF No. 35.) However, Special Master Millman denied petitioner's motion to suspend proceedings and granted respondent's motion for an extension of time to file Dr. Alexandrescu's expert report. On July 2, 2019, respondent filed an expert report from Dr. Alexandrescu. (ECF No. 40; Ex. W.)

After this case was reassigned to my docket on June 6, 2019 (ECF No. 39), I ordered petitioner to file a supplemental expert report responding to respondent's two experts or a status report otherwise indicating how petitioner wished to proceed. Petitioner indicated in a status report that, "[p]etitioner's expert feels that the best course of action for this matter would be to wait and see how the Appellate Court treats *Boatmon vs. Secretary of Health and Human Services* prior to expending his energy and the Court's resources in drafting a supplemental expert report." (ECF No. 41.) Petitioner stressed that her expert's opinions are similar to those presented in *Boatmon*. (*Id*.)

On November 7, 2019, the Federal Circuit issued its decision in *Boatmon*. 941 F.3d 1351 (Fed. Cir. 2019). Accordingly, I suspended petitioner's deadline to file a supplemental expert report and ordered petitioner to file a motion to dismiss her petition or a status report otherwise indicating how she wishes to proceed in light of the

Boatmon decision. (ECF No. 42.) Petitioner thereafter filed a status report indicating that petitioner would like to proceed with a ruling on the record.[6] (ECF No. 44.) Petitioner filed a motion for a ruling on the record on February 14, 2020. (ECF No. 46.) Respondent filed his response to petitioner's motion on March 19, 2020 and petitioner filed her reply to respondent's response to petitioner's motion on March 23, 2020. (ECF Nos. 47, 48.)

This case is now ripe for a ruling on the record.

IV. Factual History

a. Medical Records

T.A. was born via c-section at 39 weeks on March 20, 2015. (Ex. 2, p. 3; Ex. 4, p. 1.) There were no complications. (Ex. 2, p. 3.) T.A. received the Hep B vaccination on March 21, 2015. (*Id*. at 64.) Petitioner indicated that she never smoked and was negative for alcohol use. Petitioner had mostly an unremarkable pregnancy but had risks due to having undergone prior cesarean delivery and prior vaginal birth after cesarean delivery from her previous pregnancies. (*See generally*, Ex. 1.) Petitioner also had diabetes. (Ex. 2, p. 18.) Petitioner had her routine postpartum visit on May 8, 2015 and her visit was normal. (Ex. 1, pp. 8-9.)

On March 26, 2015, T.A. had her first newborn visit with Dr. Mary B. Pero. (Ex. 2, p. 3.) Dr. Pero indicated that T.A.'s perinatal history raised no pertinent complications and there were no unusual concerns during this visit. (*Id*. at 4.) During this visit, Dr. Pero discussed "appropriate newborn guidance including avoidance of second hand smoke, bed-sharing, and prone sleeping; family demonstrated understanding." (*Id*. at 5.)

T.A. had an additional well child visit on April 28, 2015. (Ex. 2, p. 28.) Petitioner was concerned that T.A. had some congestion and reported that T.A. had been congested with an occasional cough for about a week, but denied fever and fussiness. (*Id*. at 29.) Upon examination, Dr. Tori L. Demartini assessed that T.A. had normal growth, nutrition, development, and behavior. (*Id*. at 30, 32.) T.A. received a second Hep B vaccination at this visit. (*Id*. at 32, 64.)

On May 28, 2015, T.A. had her two-month well child visit with Dr. Mary Kathleen D. Kerrey and received routine childhood vaccinations (DTP, HIB, IPV, pneumococcal 13, and Rotavirus). (Ex. 2, pp. 2, 51, 59.) During this visit, Dr. Kerrey noted that T.A. had an umbilical hernia; however, assessed T.A. with normal growth, nutrition, development, and behavior. (*Id*. at 51, 53.)

[6] I have also separately determined that the parties have had a full and fair opportunity to present their cases and that it is appropriate to resolve this case without a hearing. *See* Vaccine Rule 8(d); Vaccine Rule 3(b)(2); *Kreizenbeck v. Sec'y of Health & Human Servs.*, 945 F.3d 1362, 1366 (Fed. Cir. 2020) (noting that "special masters must determine that the record is comprehensive and fully developed before ruling on the record.").

On June 2, 2015, T.A. arrived at 7:50am to the emergency department at Cincinnati Children's Hospital Medical Center with a diagnosis of cardiac arrest. (Ex. 2, p. 71.) T.A. was ventilated and unresponsive. (*Id*. at 77.) T.A.'s death was pronounced at 8:11am By Dr. Richard Ruddy and was transferred to the coroner's office. (*Id*. at 79.) It was reported by the EMS that T.A. was found down by her family. (*Id*. at 81.) Petitioner reported that T.A. was fussy the night prior and when petitioner checked on T.A. the morning after, T.A. was unresponsive and not breathing. Petitioner attempted CPR and EMS continued CPR upon arrival and finding T.A. in full arrest. (*Id*. at 85.)

Dr. Ruddy noted that T.A. "was fussy last night – no fever – and put to bed in crib on back – swaddled in blankets x 2 – this am mother awoke and went to check her and found her not breathing." (*Id*. at 87.) Additionally, he stated, "She was refractory to CPR and to epinephrine in ED – had signs of death when we did secondary survey – suggesting she [was] down for some time." (*Id*. at 88.)

Petitioner reported to Regan Kitzmiller, MSW, LSW, that T.A. was sleeping in a crib, swaddled in a blanket and petitioner placed another blanket on her. Petitioner reported that the next morning she found T.A. unresponsive with blood coming from her nose, and that T.A. was no longer swaddled in the blankets. (*Id*. at 90.)

b. Incident and Autopsy Reports

The Cincinnati Fire Department responded to petitioner's call on June 2 and arrived on scene at 7:41am. The EMS found T.A. unresponsive with frothy bloody substance from nose and mouth. (Ex. 6.) The EMS conducted CPR throughout their transfer to Cincinnati Children's Hospital Medical Center. (*Id*. at 2.)

The Hamilton County Coroner official cause of death for T.A. was sudden unexpected infant death, but the manner of death was undetermined. (Ex. 3.) Additionally, Dr. Gretel C. Stephens, deputy coroner and forensic pathologist, listed umbilical hernia, increased eosinophils in thymic medullary tissues, focus of benign subpleural left pulmonary lymphoid tissues, foci of mild chronic triaditis of the liver, and few small serous primary follicular cysts of the ovaries as additional diagnoses. (*Id*.)

Dr. Stephens indicated that many sections including the heart, lungs, thyroid, trachea, thymus, lymph nodes showed vascular congestion and the lungs also showed areas of small and larger hemorrhage with one area of benign lymphoid tissues involving subpleural tissues of the left lung. (Ex. 3, p. 5-6.) T.A.'s toxicology report results were negative. (*Id*. at 7-8.)

V. Expert Reports

a. Petitioner's Expert

Petitioner filed an expert report from neuropathologist, Douglas C. Miller, M.D., Ph.D., to support her claim. (Ex. 7.) Dr. Miller received his medical degree from University of Miami School of Medicine in 1974 and his doctorate degree in physiology and biophysics from University of Miami in 1978. (Ex. 8.) Dr. Miller is board certified in anatomic pathology and neuropathology by the American Board of Pathology. (Ex. 7, p. 3.) Dr. Miller practices as a neuropathologist at University of Missouri Healthcare and as a contract physician/consultant for the Department of Pathology at Harry S. Truman Veterans Hospital. (Ex. 8, p. 2.) Additionally, Dr. Miller currently holds a teaching position at University of Missouri School of Medicine. (*Id.* at 3). Dr. Miller has authored numerous publications relating to neurology and neuropathology. (*Id*. at 6.)

Dr. Miller has reviewed and offered his opinion supporting a "causal connection between vaccinations and SIDS in selected cases involving vulnerable infants," including testifying in at least eight different SIDS cases in this court. (Ex. 7, pp. 1-2.) Dr. Miller indicated that he "regularly performs neuropathological evaluations of infants dying suddenly and unexpectedly," and "continue[s] to learn more about the medical and scientific literature regarding the effects of vaccinations, and the mechanisms of abnormal physiology which lead to death of certain infants." (*Id*. at 2.) Through his experience as a neuropathologist consulting for various medical examiner offices, Dr. Miller indicated that he has "an extensive experience with the neuropathology of sudden infant death." (*Id*. at 3.)

In opining that vaccines contributed to T.A.'s death, Dr. Miller relied upon the above-mentioned Triple Risk Model, which "postulates that in a vulnerable infant […] an acute 'stressor' or a combination of two or more such stressors can induce apnea or hypercarbia leading to death because of the failure to have the normal homeostatic response." (*Id*. at 9.) Dr. Miller discussed the particular vulnerability regarding the defective serotoninergic network that contributes to causing sudden death in sleep. (*Id*. at 8.) He explained, relying on Dr. Hannah Kinney's study finding none or little arcuate nuclei in infants who died of SIDS, that in an infant in which the serotoninergic network is not fully functional or does not function at all, the infant cannot recover from apnea or hypercarbia during sleep, leading to death. (*Id*.)

Upon reviewing 14 autopsy slides, Dr. Miller reported that "it is correct to classify this death as one of SIDS, there is a chronic inflammatory process present in the lung tissues which could fairly be categorized as a low-grade chronic pneumonia, probably of viral etiology," which correlated with T.A.'s clinical history, but is not likely the cause of death. (Ex. 7, pp. 6-7.) With regard to the above-discussed medullary serotoninergic network deficiency, Dr. Miller explained that T.A.'s autopsy is inadequate to reveal such defect and relied instead on the statistical likelihood that such defect was present based on the fact that it is present in up to 70% of SIDS cases. (*Id*. at 9.) Dr. Miller did indicate that the slides of T.A.'s brain showed an abnormality in the hippocampus that has been

associated with SIDS, specifically dysplasia of the dentate gyrus. (*Id*. at 7.) However, this is not the same as the medullary abnormality Dr. Miller discussed as underlying the Triple Risk Model of SIDS. (*Id*. at pp. 7-8.) Instead, Dr. Miller opined that this hippocampal vulnerability may *additionally* contribute to SIDS by causing fatal seizures, often febrile seizures. (*Id*. at 12.)

Dr. Miller indicated that vaccinations, which present the immune system with antigens of infectious agents, evoke the production of cytokines, which are chemical messengers that have multiple functions including signaling the hypothalamus to elevate body temperature. (*Id*. at 10-11.) Dr. Miller opined that it is highly likely that cytokines produced in infants who received routine vaccinations can and do cross the blood brain barrier to interact with the central nervous system. (*Id*. at 11.) Additionally, Dr. Miller suggested that aluminum-based adjuvants, which are common in many vaccines, can induce increased secretion of pro-inflammatory cytokines. In a vulnerable infant with the medullary defect that suppresses the activity of the 5-HT system, SIDS ensues. The presence of a viral pneumonia had an additional effect in stimulating cytokine production which suppressed normal medullary serotoninergic neuronal activity, and T.A.'s fussy behavior was a result of the pro-inflammatory cytokines production in response to the mild pneumonia and the vaccinations. (*Id*. at 12.)

Dr. Miller also discussed risk factors leading to SIDS events including intrinsic factors such as being a premature infant, being male, being of lower socioeconomic status, being African-American, a maternal history of smoking during pregnancy, and a maternal illicit drug use or alcoholism, and extrinsic factors such as exposure to tobacco after birth, a mild illness (i.e. upper respiratory infection), prone sleeping, an excessively warm environment, fever, and co-sleeping or other unsafe sleeping condition. (*Id*.) Dr. Miller indicated regarding this case that T.A. was put to sleep on her back swaddled in a blanket with another blanket above, which "may have produced hyperthermia, setting off the cascade of events […] given the demonstrable dentate gyrus dysplasia." (*Id*. at 7-8.) Dr. Miller emphasized that SIDS is "multifactorial and does not have a single cause, which makes the evidence that might be a connection easily obscured by other factors." (Ex. 7, p. 10.) However, he further assessed the risk factors pertaining to T.A. noting that she was African American and put to sleep with blankets, and additionally, "the low grade presumably viral pneumonia which [Dr. Miller found] present in the lung slides would also be a potential cause of fever, exacerbating the warmth from the blankets. (*Id*.)

Dr. Miller stated that in most SIDS cases he has temporally associated with vaccination, the deaths occur within 72 hours of vaccination, which corresponds to the peak cytokine levels expected to be produced peripherally by the vaccination. (*Id*. at 13.) However, in T.A.'s case, where symptoms manifested four days after vaccination and death occurred five days post-vaccination, Dr. Miller opined that "the intercurrent pulmonary viral infection, itself apparently trivial, played a role in sustaining elevated pro-inflammatory cytokine levels beyond what would usually be expected from the vaccinations alone." (*Id*.)

In sum, Dr. Miller posited that T.A.'s SIDS was related to her vaccinations through the mechanistic chain involving defective medullary serotoninergic network, increased cytokines production and its interaction with the central nervous system, and especially in light of the present risk factors under the Triple Risk Model. (*Id*.)

b. Respondent's Experts

i. Andrew MacGinnitie, M.D., Ph.D.

In response, respondent filed an expert report from immunologist, Andrew MacGinnitie, M.D., Ph.D. (Ex. A.) Dr. MacGinnitie received his medical degree and doctorate degree in pathology from the University of Chicago Pritzker School of Medicine. (*Id*. at 1.) He is board certified in allergy/immunology and pediatrics. Dr. MacGinnitie currently serves as an attending physician as well as the clinical director for the Division of Immunology at Boston Children's Hospital. Additionally, he is an associate professor at Harvard Medical School. (*Id*.) Dr. MacGinnitie has been involved in the care of about 10 patients who died of SIDs and has provided expert testimony in this Program since 2015. (*Id*. at 2.)

Dr. MacGinnitie indicated that epidemiologic studies clearly show no relation between vaccination and SIDS. (*Id.* at p. 5.) Dr. MacGinnitie stated, "[w]hile epidemiology cannot prove a negative, in the case of SIDS it has identified numerous risk factors, mitigation of which has led to a 50% decline in incident. Case control studies have shown either no effect of decreased rate of SIDS, after vaccination with recent reanalysis […] suggesting there is no relationship." (*Id*.) Dr. MacGinnitie criticized Dr. Miller's reliance on several articles that do not fully support petitioner's theory, including reports that follow a limited number of cases which only "suggest[s] a chance finding." (Ex. A, pp. 5-6.) Further, Dr. MacGinnitie stressed that "[i]t is scientifically unreliable for [Dr. Miller] to discount large, sophisticated epidemiologic studies as inconclusive, but depend instead on his impression that he has seen more SIDS cases after vaccination than he would expect, although he says most of these were within 72 hours, a time frame which excludes T.A.'s death." (*Id.* at p. 6) (citations omitted).

Dr. MacGinnitie also emphasized that T.A. had a number of other risk factors for SIDS, including the likely presence of an ongoing respiratory infection, the hippocampal abnormality identified by Dr. Miller, and the use of soft bedding. (*Id.* at p. 5.) While Dr. Miller considers these risk factors as contributory and creating a cascade of events along with T.A.'s vaccinations that lead to her sudden death, Dr. MacGinnitie opined that these risk factors outweigh any potential contribution of vaccination. Dr. MacGinnitie opined that "T.A. had a number of firmly established risk factors for SIDS, so there is no need to invoke vaccination as a cause." (*Id*. at 6-7.)

Also, Dr. MacGinnitie stated that the evidence presented by Dr. Miller that vaccination triggers meaningful increases in cytokine levels is speculative at best. (*Id.* at p.5.) First, he indicated that there was no evidence of inflammation triggered by

vaccination because the articles Dr. Miller cited primarily examined in vitro cytokine production. (Ex. A, p. 7.) Additionally, Dr. MacGinnitie noted that "inflammatory cytokines can be elevated in seemingly trivial illnesses such as mild eczema and there can be significant variation (more than 10 fold) among cytokine levels in healthy individuals in the population." (*Id*. at 8.) Dr. MacGinnitie added that the evidence of a role for inflammatory cytokines in SIDS exists primarily for IL-6, not IL1β, and Dr. Miller has not presented any animal data on IL-6. (*Id*.) Lastly, he also indicated that it is possible the increased IL-6 is actually protective against the tendency of increased carbon dioxide to increase the risk of apnea. (*Id*. at 8-9.)

Dr. MacGinnitie indicated that Dr. Miller dismissed known risk factors for SIDS and instead incorrectly focuses on vaccination as a trigger in this case. (Ex. A, p. 4-5.) Therefore, Dr. MacGinnitie opined that vaccination was not related to T.A.'s tragic death and he holds this opinion to a reasonable degree of medical certainty. (*Id*. at 9.)

ii. Sanda Alexandrescu, M.D.

Additionally, respondent provided an expert opinion from pediatric pathologist and neuropathologist, Sanda Alexandrescu, M.D. (Ex. W.) Dr. Alexandrescu received her medical degree in 2004 at the University of Medicine and Pharmacy in Romania, but completed various residencies at the University of Texas Health Science Center, Boston Children's Hospital, and University of California, San Francisco. (Ex. X.) She is board certified in anatomic, clinical and pediatric pathology and in neuropathology. She currently practices as a clinician in pediatric neuropathology at Boston Children's Hospital. (Ex. W, p. 2.) Dr. Alexandrescu became the consultant neuropathologist for the Robert's Program in Sudden Infant Death associated with Harvard Medical School, where she reviews brains of children who died suddenly. (*Id*.) Additionally, Dr. Alexandrescu serves as the Chair of the Education Committee within the national Society of Pediatric Pathology.

Upon review of the 14 autopsy slides and the findings of the autopsy report, Dr. Alexandrescu indicated that there were usual signs of sudden death and no signs of trauma, electrolyte imbalance, malnutrition, or toxicity that would otherwise explain T.A.'s death. (Ex. W, p. 5.) Regarding the brain examination, given the availability of only one section, Dr. Alexandrescu found that the "dentate gyrus has areas of dispersion of the granule cells, however, there is no bilamination present." (*Id*. at 6.) She added that "[a]lthough malformation of hippocampal formation, most frequently in the form of bilamination, is present in up to half of cases of SIDS, this finding is not specific; it is also seen occasionally in epilepsy." (*Id*.) Additionally, Dr. Alexandrescu emphasized that while there is a body of literature describing the side effects of vaccination on the central nervous system, investigations have failed to discover a link between vaccination and SIDS and there is no sign of inflammation and encephalopathy in this case. (*Id*. at 7.) Dr. Alexandrescu opined that this is a case of SIDS, but she does not see any evidence of vaccination secondary effect in any of the organs examined. Moreover, she stressed that there is no demonstrated correlation between vaccination and SIDS, let alone causation. (*Id*.)

VI. Discussion

As explained above, petitioner's burden is to demonstrate by preponderant evidence each of the three *Althen* prongs for determining causation-in-fact (i.e. a medical theory, a logical sequence of cause and effect, and a proximate temporal relationship). *Althen*, 418 F.3d at 1278. Petitioner seeks to satisfy this burden via her expert, Dr. Miller, who opines that the Triple Risk Model of SIDS can be extended to include vaccination and can be applied to the circumstances of T.A.'s own death which occurred five days after routine childhood vaccinations. In this case, petitioner has failed to establish any of the three *Althen* prongs by preponderant evidence.

a. *Althen* Prong One - Dr. Miller's Extension of the Triple Risk Model to Include Vaccinations Remains Unpersuasive for the Same Reasons Discussed in *Boatmon*

Petitioner's burden under the first *Althen* prong is to provide, by preponderant evidence, "a medical theory causally connecting the vaccination and the injury." *Id*. at 1278. Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 549. Moreover, scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu v. Sec'y of Health & Human Servs*., 569 F.3d 1367, 1380 (Fed. Cir. 2009). However, to satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548; *Boatmon*, 941 F.3d at 1359.

As explained above, Dr. Miller's theory has already been addressed in multiple prior decisions, including the Federal Circuit's decision in *Boatmon* and my own prior-decision in *Downing-Powers*. In this case, as in those prior cases, I find that Dr. Miller's opinion fails to set forth a sound and reliable medical theory that could causally link T.A.'s death to her vaccinations.

First, the Federal Circuit explained in *Boatmon* that "outside of Vaccine Act litigation, vaccinations have not been identified as an exogenous stressor for SIDS." *Boatmon*, 941 F.3d at 1360. The Federal Circuit noted that petitioners' "extension of the Triple Risk Model to include vaccination-induced cytokine activity in the list of exogenous stressors" was based on "nothing more than the assertion of [petitioner's expert] Dr. Miller." *Id*. at 1361-62. I have reviewed the complete record of this case, including Dr. Miller's report and each study cited. Although the concept of the Triple Risk Model itself is not seriously debated in this case and has resulted in a significant body of literature, none of the cited literature extends the Triple Risk Model of SIDS to vaccination.[7] Moreover, both of respondent's experts, Drs. MacGinnitie and

[7] Petitioner did submit a number of publications addressing whether epidemiological evidence of an association between vaccination and SIDS exists; however, that evidence likewise does not preponderate in favor of such a relationship. Although petitioners cannot be required to come forward with epidemiological evidence, the special master may consider such evidence when filed. *Andreu*, 569 F.3d at 1378 (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325–26 (Fed. Cir. 2006). These publications do not support Dr. Miller's extension of the Triple Risk Model to include vaccinations.

Alexandrescu, affirmatively disagree that vaccinations can be implicated in the Triple Risk Model. (Ex. A, p. 5; Ex. W, p. 7.) Each separately cited literature which they characterize as refuting Dr. Miller's assertion that vaccines can be identified as exogenous stressors under the Triple Risk Model.[8] Accordingly, petitioner's theory that vaccination can be considered an exogenous stressor under the Triple Risk Model for SIDS remains both novel and based on Dr. Miller's *ipse dixit*.

In 1991 the Institute of Medicine ("IOM") examined whether there is any relationship between SIDS and the pertussis vaccine. (Christopher P. Howson, Cynthia J. Howe & Harvey V. Fineberg, eds., *Adverse Effects of Pertussis and Rubella Vaccines* (1991) (Ex. 34).) The resulting report noted that "[a]ll controlled studies that have compared immunized versus nonimmunized children have found either no association or a decreased risk of SIDS among immunized children." (*Id*. at 16 (internal citations omitted).) The IOM concluded that "[t]he evidence does not indicate a causal relation between DPT vaccine and SIDS. Studies showing a temporal relation between these events are consistent with the expected occurrence of SIDS over the age range in which DPT immunization typically occurs." (*Id*. at 17.) Dr. Miller did cite several more recent case reports originating in Germany related to a suspicion that certain hexavalent vaccines administered in Europe beginning in 2000 might be associated to sudden unexplained deaths. (B. Zinka et al., *Unexplained Cases of Sudden Infant Death Shortly After Hexavalent Vaccination*, 24 VACCINE 5779 (2006) (Ex. 31) (reporting six cases); Giulia Ottaviani, Anna Maria Lavezzi & Luigi Matturri, *Sudden Infant Death Syndrome (SIDS) Shortly After Hexavalent Vaccination: Another Pathology in Suspected SIDS?*, 448 VIRCHOWS ARCH 100 (2006) (Ex. 32) (single case report.) In 2005 von Kries et al. questioned whether unexplained deaths temporally associated with the hexavalent vaccines represented a "signal." (Rüdiger von Kries et al., *Sudden and Unexpected Deaths After the Administration of Hexavalent Vaccines (Diphtheria, Tetanus, Pertussis, Poliomyelitis, Hepatitis B, Haemophilius Influenzae Type B): Is There a Signal?*, 164 EUR J. PEDIATRIC 61 (2005) (Ex. 30).) Overall, they concluded that there is no causal relationship between sudden unexplained death and the vaccines studied; however, one of the vaccines identified as "Vaccine A" saw an unexpected temporal association to unexplained deaths following the second-year booster. This was based on three reported deaths. (*Id*. at 6-8.) They recommended enhanced surveillance. (*Id*. at 8.) A follow-up study was subsequently conducted in Italy, the second largest market for the hexavalent vaccines, over a six-year period (1999-2004), resulting in a study population of 604 unexplained deaths occurring between 31 to 729 days of age. (Giuseppe Traversa et al., *Sudden Unexpected Deaths and Vaccinations During the First Two Years of Life in Italy: A Case Series Study*, 6 PLOS ONE e.16363 (2011) (Ex. 33).) The Italian study did not confirm the "signal" found in the German study. (*Id*.) In any event, Dr. Miller opined that "[e]pidemiology, in my view, does not provide any answer to the question of a possible causal relationship between vaccinations and SIDS." (Ex. 7, p. 10.)

[8] Mechtild Vennemann et al.., *Sudden Infant Death syndrome: No Increased Risk After Immunisation*, 25 VACCINE 336 (2007); Mechtild Vennemann et al., *Do immunisations reduce the risk for SIDS? A meta-analysis*, 25 VACCINE 4875 (2007); Ronny Kuhnert et al., *Reanalyses of Case-Control Studies Examining the Temporal Association Between Sudden Infant Death Syndrome and Vaccination*, 30 VACCINE 2349 (2012); Linda E. Silvers et al., *The epidemiology of Fatalities Reported to the Vaccine Adverse Event Reporting System 1990-1997*, 10 PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 279 (2001); AAP Task Force on Sudden Infant Death Syndrome, *SIDS and Other Sleep-Related Infant Deaths: Updated 2016 Recommendations for a Safe Infant Sleeping Environment*, 138 PEDIATRICS e20163298 (2012)) (EX. A, p. 5); Katherine Duszynski et al., *Use of Different Combination Diptheria-tetanus-acellular pertussis Vaccines Does Not Increase Risk of 30-day Infant Morality. A Population Based Linkage Cohort Study Using Administrative Data From the Australian Childhood Immunosation Register and the National Death Index*, 37 VACCINE 280 (2019); Y. Tony Yang, Jana Shaw, *Sudden Infant Death Syndrome, attention-Deficit/Hyperactivity disorder and Vaccines: Longitudinal Population Analyses*, 36 VACCINE 595 (2018); Kathleen Stratton et al., *Immunization Safety Review: Vaccination and Sudden Unexpected Death in Infancy,* Institute of Medicine Immunization Safety Review Committee (2003).
(Ex. W, p. 7)

As I previously discussed in *Downing-Powers*, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Downing-Powers*,2020 WL 4197303 at *13 (quoting *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 743 (2009) (citation omitted); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013). In that regard, the fact that petitioner's theory ultimately rests upon Dr. Miller's *ipse dixit* extrapolation of the Triple Risk Model is especially significant because the evidence underlying his opinion that vaccines can act on the serotoninergic network is also weak.

This relates to the second relevant point raised by the Federal Circuit in *Boatmon*. As in that case, petitioner has not satisfactorily demonstrated that vaccines produce cytokines that act on the 5-HT receptors in a manner consistent with the Triple Risk Model of SIDS. Dr. Miller continues to rely largely on animal-model studies, three of which were explicitly rejected by the Federal Circuit in *Boatman*. Specifically, as in *Boatmon*, Dr. Miller relies in this case on two pig studies, by Stoltenberg et al., and Frøen et al., respectively, and one rat study by Brambilla et al.[9] He additionally cites an additional piglet study by Tang et al., and a further rat study by Li et al.[10] I find that these studies are insufficient to show that a cytokine response would affect the 5-HT receptors as alleged *in vivo*. Dr. MacGinnitie is persuasive in explaining in particular that the piglet studies "are of questionable relevance given the methods used." (Ex. A, p. 8.) Most notably, he indicated that the piglets were administered 20 pmol[11] of IL-1β, which is not physiologic. (*Id*.)

Dr. Miller cited Kashiwagi, et al, for the proposition that vaccinations have been shown to increase IL-β in humans and contended without elaboration that "the amounts [IL-1β] of used [in Frøen and Stoltenberg], I have calculated, are not greater than the higher levels of cytokines evoked by vaccines in vitro as reported by Kashiwagi, et al." (Ex. 7, p. 12.) However, whereas Dr. Miller did not disclose his calculation, Dr. MacGinnitie explained that the amount of IL-1β administered in the Frøen study

[9] L. Stoltenberg et al., *Changes in Apnea and Autoresuscitation in Piglets After Intravenous and Intrathecal Interleukin-1β Injection*, 22 J. PERINAT MED. 421 (1994) (Ex. 43); J.F. Frøen et al., *Adverse Effects of Nicotine and Interleukin-1β on Autoresuscitation After Apnea in Piglets: Implications for Sudden Infant Death Syndrome*, 105 PEDIATRICS E52 (2000) (Ex. 44); D. Brambilla et al., *Interleukin-1 Inhibits Firing of Serotonergic Neurons in the Dorsal Raphe Nucleus and Enhances GABAergic Inhibitory Post-Synaptic Potentials*, 26 EUR. J. NEUROSCIENCE 1862 (2007) (Ex. 45).

[10] Samantha Tang, Rita Machaalani & Karen A. Waters, *Brain-Derived Neurotrophic (BDNF) and TrkB in the Piglet Brainstem After Post-Natal Nicotine and Intermittent Hypercapnic Hypoxia*, 1232 BRAIN RESEARCH 195 (2008) (Ex. 46); Qingqing Li, *Neonatal Vaccination with Bacillus Calmette-Guerin and Hepatitis B Vaccines Modulates Hippocampal Synaptic Plasticity in Rats*, 288 J. NEUROIMMUNOLOGY 1 (2015) (Ex. 50).

[11] Abbreviation for "picomole" a unit of measurement used to determine the molecular weight of a substance. In this case, 20 pmol of IL-1β is equal to 350 nanograms or .0000035 grams. (EX. A, p. 8.)

represents a concentration of 2.33 ng/ml, 1,000-fold higher than the highest concentration of IL-1β observed by Kashiwagi, et al., which he noted to be 1.53 pg/ml.[12] Moreover, Kashiwagi, et al, has been discussed in several prior SIDS cases, including my own prior decision in *Downing-Powers*, and has not been found to support the idea that cytokines produced peripherally in response to vaccination could negatively impact the brain.[13] *See, e.g., Downing-Powers*, 2020 WL 4197303 at *13; *Dean v. Sec'y of Health & Human Servs*., No. 13-808V, 2017 WL 2926605, at *17 (Fed. Cl. Spec. Mstr. June 9, 2017); *Copenhaver, supra,* at *9-14*; Cozart, supra,* at *6-7. And, in any event, the Federal Circuit has also now explicitly rejected the Kashawagi study as the type of additional evidence that could distinguish a case such as this case from the prior *Boatmon* case. *Nunez*, 2020 WL 5087990, at *2.

Moreover, even where cytokines are shown to be present in the central nervous system of humans, the evidence still does not implicate vaccinations. This was likewise an issue directly addressed by the Federal Circuit. *Boatmon*, 941 F.3d at 1361 (noting that during oral argument petitioner was asked to distinguish between the presence of cytokines and the function of cytokines). The studies relied upon by Dr. Miller do not establish that cytokines are present for the reasons Dr. Miller asserts. For example, one of the studies cited by Dr. Miller found evidence of increased levels of the cytokine Interleukin-2 ("IL-2") within the brainstems of SIDS decedents. (Hazim Kadhim et al., *Interleukin-2 as a Neuromodulator Possibly Implicated in the Physiopathology of Sudden Infant Death Syndrome*, 480 NEUROSCIENCE LETTERS 122, 123 (2010) (Ex. 49, p. 2).) I previously explained in *Downing-Powers*, however, that among the post-mortem brain tissue samples were eighteen infants experiencing SIDS as well as ten controls that died of known, diverse causes, including infectious, hemodynamic, metabolic, severe congenital, or other serious conditions. *Downing-Powers*, 2020 WL 4197303, at *15. Although the study authors suggested that their results evidenced a "central neuro-cytokine connection" in SIDS, they could not distinguish from among the wide range of "various biological stressors" (including infectious/inflammatory,

[12] Note the change in the unit of measure. Dr. MacGinnitie's conclusion that there is a 1,000-fold difference reflects that one nanogram (ng) is equal to (10^{-9}) grams while a picogram (pg) is equal to (10^{-12}) grams. Dr. MacGinnitie's calculation is based on at least some unsourced assumptions. For example, he makes an assumption that a pig's blood represents about 7% of its body weight, similar to humans. (Ex. A, p. 8.) However, these assumptions are unrebutted and at least provide a basis upon which to scrutinize the calculation. Dr. Miller on the other hand never disclosed the manner of his competing calculation. (Ex. 7, p. 12.)

[13] In *Downing-Powers*, respondent's expert, Dr. McCusker, persuasively opined that Kashiwagi study does not support Dr. Miller's theory because it only reflects cytokine production in the periphery, as is expected in vaccination. Moreover, like Dr. MacGinnitie in this case, Dr. McCusker (who also opined in *Boatmon*) stressed that Kashiwagi, et al, further illustrates that the *in vivo* cytokine production in response to vaccine is "orders of magnitude less" than what was used in the animal studies the animal studies relied upon by Dr. Miller. *Downing-Powers*, 2020 WL 4197303 at *13. Dr. McCusker indicated that the animal studies required cytokine levels over 1,000-times greater than what is produced in response to vaccine and therefore have little relevance in a clinical setting. *Id.* at *14. She also indicated that Kashiwagi, et al, found that IL-1β was not elevated by 48-hours post-vaccination. *Id.* at *13.

ischemic/anoxic, immune conditions, and metabolic disorders) that affected both the SIDS and non-SIDS study groups. (*Id*.)[14]

A different study cited by petitioner examined the presence of a different cytokine – Interlueken-6 ("IL-6") – and found "abnormal IL-6 [receptor] expression in the arcuate nucleus in SIDS cases," but noted that 44% of those cases had mild infections prior to death. (Ingvar Jon Rognum et al., *Interleukin-6 and the Serotonergic System of the Medulla Oblongata in the Sudden Infant Death Syndrome*, 118 ACTA NEUROPATHOLOGY 519, 529 (2009) (Ex. 38, p. 8).) The authors concluded that the deaths were "potentially induced by the combined effect of prone position and mild infection." (*Id*.) Dr. MacGinnitie further stressed that the study authors postulated that "[t]he increased expression of the IL-6R in the arcuate nucleus may be a compensatory mechanism as defective arcuate neurons may require excessive IL-6 stimulation in order to respond to altered CO2 levels." (*Id*. at 9.) Dr. MacGinnitie argues that this suggests a protective effect. (Ex. A, p. 9.) But in any event, it would also suggest that the presence of these cytokines evidences the biological process proposed by the Triple Risk Model itself rather than separately evidencing that a vaccine reaction triggered that process.

In fact, consistent with Dr. MacGinnitie's opinion in this case, it has been suggested in other cases that Dr. Miller's reliance on cytokine signaling as the manner in which vaccination would lead to SIDS is actually incompatible with the underlying brainstem defect that is hypothesized to contribute to death via the Triple Risk Model. In *Nunez*, the Federal Circuit observed that "the Special Master found that, not only does the evidence of J.J.'s defective brainstem not support Dr. Miller's theory, it actually cuts against the theory. That finding was based on the logical chain of evidence demonstrating that Dr. Miller's theory is based on the premise that cytokines affect the medullary serotonin system by sending messages through functioning—*i.e.*, non-defective—receptors in the brain." *Nunez*, 2020 WL 5087990, at *3. The Circuit held that "[i]t was thus logical and reasonable for the Special Master to find that, because J.J.'s brainstem was defective, the medullary serotonin system would not be affected by the cytokines in the way that Dr. Miller proposed and that '[t]he ultimate cause of death is the cause of the increased CO2 that leads to the cessation of breathing and not the cytokines' effect on the arousal system.'" *Id.* In the decision below, the *Nunez* special master had explained that the cytokines may instead be a marker for the inability to breath or may relate to the mechanism for arousal. *Nunez v. Sec'y of Health & Human Servs.*, No. 14-863V, 2019 WL 2462667, at *41 (Fed. Cl. Spec. Mstr. Mar. 29, 2019).

Finally, it does bear stressing, especially in light of the points discussed above, that Dr. Miller himself characterized his theory as merely "plausible." (Ex. 7, p. 10.) The *Boatmon* Court stressed, citing the 2010 Federal Circuit decision *Moberly v. Secretary of Health & Human Services*, 592 F.3d 1315 (Fed. Cir. 2010), that "[w]e have consistently rejected theories that the vaccine only 'likely caused' the injury and reiterated that a 'plausible' or 'possible' causal theory does not satisfy the standard.'" *Boatmon*, 941 F.3d at 1360.

[14] Although Dr. Miller relied on this same study in this case as he did in *Downing-Powers,* petitioner has only filed the abstract of the study in this case. (Ex. 49).

In sum, Dr. Miller's opinion in this case remains very similar to the opinion he presented in *Boatmon* and continues to suffer the same fatal weaknesses. Thus, although the record of this case is not identical, Dr. Miller's opinion in this case remains unpersuasive for the same reasons discussed in *Boatmon*.

b. *Althen* Prong Two – Logical Sequence of Cause and Effect

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). However, medical records and/or statements of a treating physician do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. *See* Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing ... that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

Here, even assuming as a matter of general causation that vaccinations could be considered an exogenous stressor pursuant to the Triple Risk Model, Dr. Miller has also failed to persuasively describe a logical sequence of cause and effect explaining pursuant to his theory how any of T.A.'s vaccinations could have contributed to her SIDS via that Triple Risk Model for two significant reasons – the absence of evidence of a medullary defect in T.A.'s brain and the presence in this case of pneumonia

i. T.A.'s Own Pathology Is Inadequate to Support Petitioner's Theory

First, despite his identification of dysplasia of the dentate gyrus, Dr. Miller has failed to demonstrate the underlying medullary defect that is necessary to his explanation of the sequence of cause and effect leading to T.A.'s death. This was a significant issue raised by the Federal Circuit relative to the *Boatmon* petitioner's case under an *Althen* prong two and, notwithstanding petitioner's argument to the contrary, also presents an issue in this case for the same reason.[15] *Boatmon v. Sec'y of Health and Human Servs.*, 941 F.3d 1351, 1356-57 (Fed. Cir. 2019).

In her motion reply, petitioner is critical of respondent for "want[ing] it both ways. They want this Court to accept that T.A.'s brain and situation was exactly the same as the poor child in *Boatmon* yet it was different enough that the objective abnormality found in her brain was the alternative cause of her death. You cannot have it both ways.

[15] As noted above, in *Nunez* the Federal Circuit indicated that it was not an abuse of discretion for the special master to find that the presence of a medullary defect actually "cut against" Dr. Miller's explanation for vaccine-related cytokine signaling as a cause of SIDS. *Nunez*, 2020 WL 5087990, at *3. Because that relates to the viability of petitioner's theory that vaccines can act as exogenous stressors pursuant to the Triple Risk Model, that raises an *Althen* prong one question. In this section I set that specific consideration aside and examine how T.A.'s own brain pathology fits within the framework of Dr. Miller's theory as he has presented it.

It was either the same or it was different. In this case we have a baby who died with an objective abnormality found in her brain that made her more susceptible to death. Arguing that the vaccines caused the death of an infant with a pre-existing condition that made her more susceptible to death is absolutely reasonable and allowed under the law." (ECF No. 48, pp. 1-2.)

Critically, however, petitioner's theory applying the Triple Risk Model (via Dr. Miller's own description) is not predicated on the presence of *any* brain defect. It is predicated on the idea of a defect of the medullary serotonergic network, because that part of the brain has been associated with arousal from apnea and has been shown to be the subject of prior studies that specifically link that defect to the Triple Risk Model relied upon by Dr. Miller. (Ex. 7, pp. 8-9.) That particular defect was also at issue in the prior *Boatmon* case. *Boatmon v. Sec'y of Health & Human Servs*., No. 13-611V, 2017 WL 3432329 (Fed. Cl. July 10, 2017), review granted, decision rev'd, 138 Fed. Cl. 566 (2018), aff'd on other grounds, 941 F.3d 1351 (Fed. Cir. 2019). As in the *Boatmon* case, Dr. Miller does not identify this defect as present in this case based on T.A.'s own pathology, but instead opines based on the statistical likelihood that SIDS victims have such a defect.[16] (Ex. 7, p. 9.) Accordingly, just as in *Boatmon*, this statistical probability does not serve as evidence that T.A. actually had the underlying vulnerability suggested by the Triple Risk Model.

Respondent, in contrast, raises the issue of an alternative cause based on a separate defect in the hippocampal region, which was first identified by Dr. Miller and subsequently discussed by respondent's expert as well. (ECF No. 47, p. 3.) Specifically, Dr. Miller indicated that the available pathology in this case indicates an abnormality of the hippocampus of "extensive" dysplasia of the dentate gyrus. (Ex. 7, p. 7.) Dr. Alexandrescu opined that these findings are suggestive of, but not definitive evidence of, a hippocampal deformity, which represents a non-specific finding that is present in up to half of SIDS cases. (Ex. W, p. 6.) In discussing this finding, Dr. Miller explains that this specific condition has been shown by Dr. Kinney to contribute to SIDS in the context of epilepsy within a hypothesis of "Sudden Unexpected Death in Epilepsy" or "SUDEP." (Ex. 7, p. 7.)

As Dr. Miller explains it, this hippocampal vulnerability leads to seizures following "ascending input from the brainstem, originating in the medullary arousal centers" and "[t]his chain of hypotheses ties these hippocampal abnormalities to the previously documented brainstem, particularly medullary abnormalities in the large majority of SIDS cases." (*Id*.) Dr. Miller's report makes clear that his opinion is that the effect of the

[16] Specifically, Dr. Miller explains: "For T.A., I can make no statement about the arcuate nuclei, or about any subtle or worse focal dysplasia of one or both inferior olivary nuclei, which when present are indications of a developmental abnormality in medullary structures derived from the embryonic rhombic lip; obviously, this is so because there are no sections of this or any other part of the brain other than one temporal sample from this autopsy. In the published studies from Kinney and others already cited, this is believed to be the underlying origin of the various 5HT neuronal system abnormalities in most SIDS brains, and on a statistical basis (if this is 70% of SIDS cases) it is most likely that T.A. had such an abnormality as the underlying vulnerability which made SIDS a possible outcome." (Ex. 7, p. 9.)

dentate gyrus dysplasia, if anything, operates as a further vulnerability combining with the medullary defect otherwise implicated by the Triple Risk Model. According to Dr. Miller's opinion, the presence of dysplasia of the dentate gyrus does not substitute for evidence of a defect in the medullary serotonergic network when applying the Triple Risk Model. Specifically, Dr. Miller opined that "most likely" the suspected 5HT neuronal system abnormality is "the underlying vulnerability which made SIDS a possible outcome" and that "the alteration of serotonergic activity in the brainstem has effects through projections to the hippocampi, and the deleterious effects of such alterations may also trigger febrile seizures with fatal consequent if one or the other dentate gyrus is maldeveloped." [17] (*Id*. at 9, 12.) Nowhere in his report did Dr. Miller attempt to link SIDS to vaccination without invoking the mechanism of a medullary defect.

Nonetheless, Dr. Miller also suggests that the hypothesis of SUDEP may potentially provide a separate explanation for T.A.'s SIDS that need not implicate vaccination. Specifically, Dr. Miller indicated that the fatal seizures hypothesized by SUDEP "can be triggered by fever (or perhaps other causes of hyperthermia, such as excessive warmth in the bed)." (Ex. 7, p. 7.) Thus, he opined that "[f]or this case I think there is no evidence of an 'accidental overlay' or asphyxiation, and so as stated I believe this is a case of SIDS, but the mother told either EMS or the Emergency Room personnel that the child was put to sleep on her back swaddled in a blanket with another blanket above that, which goes against current safe sleep recommendations and may have produced hyperthermia, setting off the cascade of events described above given the demonstrable dentate gyrus dysplasia." (*Id*. at 7-8.)

[17] This is consistent with the cited literature. In 2014 the Kinney research group hypothesized that hippocampal abnormality may be a marker of the type of underlying vulnerability implicated by the Triple Risk Model. (Hannah C. Kinney et al., *Dentate Gyrus Abnormalities in Sudden Unexplained Death in Infants: Morphological Marker of Underlying Brain Vulnerability*, 129 ACTA NEROPATHOLOGICA 65, 73 (2015) (Ex. 14, p. 9.).) However, this was based on the connection of the hippocampus to brainstem sites that regulate autonomic function and respiration. (*Id*. at 10.) The thinking was that temporal lobe epilepsy may contribute to autonomic seizures and apnea. (*Id*.) In their most recent work, the Kinney group explained that none of the deaths studied have been witnessed and there is not a one-to-one relationship between this type of death and a history of febrile seizures. (Marco M. Hefti et al., *Hippocampal Malformation Associated with Sudden Death in Early Childhood: a Neuropathologic Study*, 12 FORENSIC SCI. MED. PATHOLOGY 14, 23 (2016) (Ex. 16, p. 10.).) Accordingly, the authors believe febrile seizures should be considered a risk factor rather than a cause for sudden death and that understanding the relationship between sleeping and waking remains critical to understanding the etiology and pathogenesis of SIDS. (*Id*.) None of the cited literature includes vaccines in the discussion of febrile seizures. (Hannah C. Kinney et al., *Sudden Death, Febrile Seizures, and Hippocampal and Temporal Lobe Maldevelopment in Toddlers: A New Entity*, 12 PEDIATRIC DEV. PATHOLOGY 455 (2012); Michael L. Rodriguez et al., *Hippocampal Asymmetry and Sudden Unexpected Death in Infancy: A Case Report*, 8 FORENSIC SCI. MED. PATHOLOGY 441 (2012); Hannah C. Kinney et al., *Dentate Gyrus Abnormalities in Sudden Unexplained Death in Infants: Morphological Marker of Underlying Brain Vulnerability*, 129 ACTA NEROPATHOLOGICA 65 (2015); Marco M. Hefti et al., *Sudden Unexpected Death in Early Childhood: General Observations in a Series of 151 Cases*, 12 FORENSIC SCI. MED. PATHOLOGY 4 (2016); Marco M. Hefti et al., *Hippocampal Malformation Associated with Sudden Death in Early Childhood: a Neuropathologic Study*, 12 FORENSIC SCI. MED. PATHOLOGY 14 (2016); Hannah C. Kinney et al., *Hippocampal Formation Maldevelopment and Sudden Unexpected Death Across the Pediatric Age Spectrum*, 75 J. NEUROPATHOLOGY & EXPERIMENTAL NEUROLOGY 981 (2016) (Ex. 7, p. 14))

This suggestion by Dr. Miller of a direct relationship between hyperthermia and death in the setting of dentate gyrus dysplasia makes no reference to vaccination and provides an alternate explanation by petitioner's own expert suggesting that T.A.'s own brain pathology could provide evidence supporting SIDS without supporting a logical sequence of cause and effect linking her vaccinations to her death via the Triple Risk Model. Accordingly, there is nothing inherently disingenuous in respondent both arguing that petitioner has not met her burden vis-à-vis demonstrating a medullary defect consistent with petitioner's proffered theory of vaccine causation while also arguing that the hippocampal defect could constitute an alternative explanation of SIDS unrelated to vaccination. In prior cases, the Federal Circuit has allowed respondent to present evidence regarding SIDS as factor unrelated to vaccination. *See, e.g.*, *Doe/11*, 601 F.3d at 1351.

In sum, Dr. Miller has not established the presence of a medullary serotoninergic network defect in this case – as called for by his own theory – by preponderant evidence. Nor has he otherwise explained, absent a medullary defect, how T.A.'s vaccines contributed to her death in the context of her own brain pathology. Accordingly, petitioner cannot meet her burden of proof under *Althen* prong two based on T.A.'s brain pathology regardless of whether I accept respondent's competing assertion that the hippocampal findings suggest an alternative explanation.

ii. In Applying the Triple Risk Model, Dr. Miller Establishes Pneumonia as a More Likely Exogenous Stressor

In light of petitioner's proffered theory, petitioner's inability to demonstrate the presence of an underlying vulnerability is fatal to Dr. Miller's opinion seeking to apply the Triple Risk Model. However, even assuming *arguendo* that petitioner did establish the presence of an underlying vulnerability, Dr. Miller's opinion makes a stronger case for pneumonia being the relevant exogenous stressor within the Triple Risk Model than any vaccination.

Specifically, Dr. Miller explained that "while I think it is correct to classify this death as one of SIDS, there is a chronic inflammatory process present in the lung tissues which could fairly be categorized as a low-grade chronic pneumonia, probably of viral etiology. As noted, this correlates with the clinical history, and likely also accounts for the lymphoid hyperplasia in the paratracheal lymph nodes." (Ex. 7, pp. 6-7.) Dr. Miller explained that this viral pneumonia does not explain T.A.'s death to the extent that "this finding does not alter the interpretation as SIDS" (Ex. 7, p. 7), but also included viral upper respiratory infection as one of the ways in which the Triple Risk Model can explain a death such as T.A.'s (Ex. 7, p. 12). Dr. MacGinnitie likewise agrees that viral infection is associated with SIDS, quoting a review by Dr. Kinney that indicates that "in approximately half of SIDS cases, the infants have a seemingly trivial infection around the time of death." (Ex. A, p. 6 (quoting Kinney & Thach, *supra*, at Ex. D).) Moreover, Dr. MacGinnite further specifically opined that the pneumonia was a more likely contributor to T.A.'s own death from SIDS than vaccination. (Ex. A, p. 6.)

Indeed**,** Dr. Miller's above-discussed, merely "plausible," theory for how vaccines can act as exogenous stressors within the Triple Risk Model is based on his extrapolation from stronger evidence relating to a generally accepted association between upper respiratory infections and SIDS.[18] In explaining the mechanism of his theory, Dr. Miller indicated that "a major hint comes from the evidence that otherwise innocuous upper respiratory viral infections are associated with SIDS in vulnerable infants." (Ex. 7, p. 10.) Dr. Miller disputes that this association stems from possible, unrelated airway obstruction from mucus. (*Id*.) Instead, he opines that:

> Most of the medical literature, including that coming from the Kinney laboratory and her collaborators elsewhere, suggest that cytokines produced in response to the infection may interact with, and suppress, the activity of the 5HT system in the medulla . . . In a normal infant with a normal medullary neuronal 5HT network, such suppression is likely insufficient to cause death, but in an infant with a defective medulla the additional suppression by cytokines added to the existing inadequate system for responding to apnea, hypoxia, or hypercarbia, can indeed lead to death.

(*Id.*)

> More to the point, Dr. Miller indicated with regard to T.A.'s case that
>
> T.A. was put to sleep with blankets. Soft bedding, blankets, and prone sleep position are all thought to create a risk for trapping carbon dioxide exhaled by the infant in an air pocket about his or her mouth and nose, leading to "re-breathing" of excess CO2 and thus increased serum CO2; whether the blankets ever covered T.A.'s face is not discussed in the records, but the issue of excessive warmth is clearly raised by the blankets. Furthermore, the low grade presumably viral pneumonia which I have described as present in the lung slides would also be a potential cause of fever, exacerbating the warmth from the blankets.

(*Id*. at 9.)

He further opined that "[i]n T.A., the presence of a viral pneumonia, otherwise likely clinically insignificant, would have most probably had additional effects in stimulating cytokine production, in particular pro-inflammatory cytokines including interlueken 1-beta, of particular importance in terms of suppression of normal medullary serotoninergic neuronal activity." (*Id*. at 11.)

[18] For example, Rognum, et al, cited by Dr. Miller as evidence of cytokine Il-6 being present in the arcuate nucleus, actually attributed the SIDS deaths examined in that study, not to vaccination, but to prone sleeping combined with mild infection. (Ex. 38, p. 11.) Moreover, as Dr. Miller acknowledged and Dr. MacGinitie stressed, Dr. Kinney's group has also specifically identified mild upper respiratory infections as exogenous stressors pursuant to the Triple Risk Model. (Ex. A, pp. 3-4.)

Thus, although Dr. Miller does ultimately seek to characterize the pneumonia and vaccinations as working in combination to cause T.A.'s death, he has not persuasively demonstrated that the vaccination would have any role in the process. As explained above, Dr. Miller's theory that vaccinations act as exogenous stressors is premised on the much stronger evidence that infections are generally accepted as exogenous stressors via the Triple Risk Model to contribute to SIDS independent of Dr. Miller's suspicion of vaccine-causation. Moreover, Dr. Miller has provided an explanation of exactly how warmth and rebreathing related to T.A.'s bedding and potential pneumonia-related fever represents a logical sequence of cause and effect explaining T.A.'s death in the context of the Triple Risk Model. And indeed, he was clear in explaining that even "an otherwise 'trivial' or 'mild' upper respiratory infection" can be considered a risk factor for SIDS. (Ex. 7, p. 7.)

Based on this, and having examined Dr. Miller's report in full, he has not persuasively explained why he nonetheless effectively opines that the death would not have occurred but for vaccination.[19] In that regard respondent persuasively argues that "known SIDS risk factors were present in this case, which can independently explain the cause of T.A.'s unfortunate death, such as the use of soft bedding and evidence of viral infection." (ECF No. 47, p. 3.)

iii. *Althen* Prong Three – Dr. Miller has Not Persuasively Explained How His Theory Can be Applied to a Death Occurring Five Days Post-Vaccination

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11–355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30,

[19] Notably, Dr. Miller indicated that "[t]o summarize and repeat the point, in an infant whose medulla is not properly developed and has a defective serotoninergic network *who has an upper respiratory viral infection, or who has received vaccines*, has had production of a range of cytokines upregulated in the periphery; these enter the bloodstream, and are predictably transported across the [blood brain barrier] by an active mechanism." (Ex. 7, p. 12.) He further explained "and so SIDS can ensue, whereas an infant with a normal medullary 5HT system would survive such an event *whether from infection or vaccination*." (*Id.*) Although it is apparent from Dr. Miller's report as a whole that his opinion is that the vaccination contributed to causing SIDS in T.A.'s specific case, it is nonetheless highly relevant that in this passage Dr. Miller discusses the role of vaccinations and infections in the Triple Risk Model in the disjunctive. This is consistent with Dr. Miller's acknowledgment of the ability of mild upper respiratory infections to cause SIDS independent of vaccinations.

2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Here, Dr. Miller opines:

> The timing of this death requires a brief extra analysis. For most of the SIDS deaths I have seen with a temporal relationship to vaccinations, the deaths have occurred with[in] less than 72 hours of vaccination, and this more or less corresponds to the peak cytokine levels expected to be produced peripherally by the vaccination. In the case of T.A., symptoms ("fussiness") did not appear, or were not recognized, prior to almost four days after vaccination, and death was just some hours short of five days. It seems likely to me that the intercurrent pulmonary viral infection, itself apparently trivial, played a role in sustaining elevated pro-inflammatory cytokine levels beyond what would usually be expected from the vaccinations alone.

(Ex. 7, p. 13.)

As explained in section VI(a) above, Dr. Miller's theory that vaccines can act as an exogenous stressor via the Triple Risk Model is not generally accepted and the Triple Risk model does not contemplate a temporal relationship between vaccination and SIDS. Accordingly, it is difficult to assess Dr. Miller's proposed temporal relationship. However, by his own description, the timing in this case is not consistent with his own previously expressed rationale of correlating deaths to peak post-vaccination cytokine production based on a 72-hour period. Rather, there is some suggestion here that the timing is more likely to be consistent with a causal role for T.A.'s pneumonia than her vaccinations, especially in light of my finding in section VI(b)(ii) above, that Dr. Miller's opinion supports a finding that T.A.'s pneumonia was sufficient to act alone as a fatal, exogenous stressor. Thus, given the medical understanding of SIDS, Dr. Miller's above-quoted opinion does not provide preponderant evidence that it is medically acceptable to infer that T.A.'s death, occurring five days following her vaccinations, was caused by those vaccinations.

In any event, a temporal relationship alone cannot establish causation. *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that a "temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury."). Thus, petitioner's failure to meet prongs one and two means that petitioner cannot be compensated. *Hibbard v. Sec'y of Health & Human Servs.*, 698 F.3d 1355, 1364-65 (Fed. Cir. 2012) (holding the special master did not err in resolving the case pursuant to Prong Two when respondent conceded that petitioner met Prong Three).

VII. Conclusion

In light of all of the above and in consideration of the record as a whole, I find that petitioners have failed to meet their burden under the *Althen* test. Dr. Miller did not provide a sound and reliable theory of causation linking T.A.'s death to any of her

vaccinations nor persuasively apply his proposed theory with regard to the timing and logical sequence of events occurring in this specific case.

T.A.'s unexplained death is tragic and a profound loss for her family. Petitioner has my deepest sympathy. However, upon my review of petitioner's claim, petitioner has not established by preponderant evidence that any of T.A.'s vaccinations caused her death. Accordingly, this petition is DISMISSED.[20]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[20] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.